UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 19, 2013

MEMORANDUM

SUBJECT: Review of [redacted] Draft Protocol for a Reproduction/ Developmental Toxicity Screening Test of [redacted] Administered by Oral Gavage in Crl:CD1(ICR) Mice [P-09-0291]

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[redacted]

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CONCLUSION

This protocol provides a thorough description of the proposed reproduction/ developmental toxicity screening test. A few comments and questions are listed in this memorandum.

1. BACKGROUND

REFERENCE:

[redacted] 2013. Draft Protocol for a Reproduction/ Developmental Toxicity Screening Test of [redacted] Administered by Oral Gavage in Crl:CD1(ICR) Mice. For: Testing Facility Study No. [redacted]. November 21.

[redacted]

TEST MATERIAL PURITY/COMPOSITION: The purity was not stated in the protocol, but the protocol noted that the characterization and stability was analyzed by the Sponsor or Sponsor subcontractor.

SPONSOR:

[redacted]

TESTING FACILITY:

[redacted]

II. COMMENTS AND CONCLUSIONS

The protocol provides a thorough description of the reproduction/developmental toxicity screening test to be conducted according to OECD Test Guideline 421 and EPA Health Effects Test Guideline OPPTS 870.3550 as modified according to the specifications in a signed consent order for this PMN from October 5, 2009. Any unspecified procedures are assumed to be in accordance with the OECD/OPPT guidelines. EPA has three main comments:

- It is not clear whether the middle dose (0.5 mg/kg bw/day) will result in toxicity based on the discussion in the protocol. It would be appropriate to choose a middle dose that would show some toxicity to at least observe any possible trends in effects between the middle and highest doses. Perhaps a value of 0.75 mg/kg bw/day would result in a dose that results in some toxicity that is not severe. EPA

notes that this is 7.5 times higher than the lowest dose (larger dose spacing than recommended by guidelines) and yet, it seems that it might be more useful than 0.5 mg/kg bw/day for evaluating the potential effects of this compound. Alternately, the sponsor could provide EPA with more details from the cited range-finding studies (e.g., exposure duration and incidence of effects by dose) so that EPA could more effectively assist in evaluating an appropriate dosing strategy.

- The protocol notes the proposal to use psychological enrichment during the study. Although this seems reasonable, it would be useful to know whether other studies at [redacted] have routinely used such enrichment. If not, comparisons between the results of this test and other studies with respect to control responses, for example, could be limited.

- The proposed indices to be measured appear to be standard. Nevertheless, in the final study report, the sponsor should clearly define the indices by describing the data used as well as how the data are combined to calculate each index (e.g., mating index).